

The adjustments for approximating human equivalent slope factors use the EPA cross-species scaling methodology. Using this approach, time weighted daily average doses are converted to HEDs on the basis of  $BW^{3/4}$  scaling, citing USEPA (1992). According to USEPA (1992),  $BW^{3/4}$  is used as a default in the absence of chemical-specific information and is surrounded by considerable uncertainty – individual chemicals can deviate from this value by two orders of magnitude or more in either direction. It encourages the use of information on mode of action, reaction rates, pharmacokinetics, and other factors as appropriate to derive a chemical-specific scaling factor, if sufficient data are available. For example, it states, “Clearly, when data on metabolic conversion are available in a particular case, they should be used in preference to the  $W^{3/4}$  default.” Given that cross-species scaling is an important source of uncertainty in the development of the oral cancer slope factor, the panel recommends additional discussion and justification why the default is the best choice given what is known about BaP. The panel suggests that this discussion include an explanation why, in EPA’s opinion, the caveat in USEPA (1992) on using  $BW^{3/4}$  scaling when the active carcinogen is a reactive metabolite does not apply to BaP. Also, alimentary tract tumors (larynx, esophagus, forestomach) arguably meet the definition of portal of entry effects, and additional discussion of their scaling in this context is needed. The matter of appropriate scaling for carcinogenic responses specifically at portals of entry has not received much attention. Recent guidance (USEPA 2011) on allometric scaling for oral reference doses recommends the use of  $BW^{3/4}$  as a “pragmatic and reasonable approach” for portal of entry effects, but acknowledges that the utility of this scaling factor for portal of entry effects has not been systematically evaluated and presents an alternative approach that scales on mass/surface area (analogous to inhalation exposure). At a minimum, the discussion should make clear the extent of scientific support for the scaling factor, not in general (which is clearly described in USEPA 1992; 2011; and others), but for BaP specifically.

Also, for transparency, the impact of the change in allometric scaling from  $BW^{2/3}$  used in the 1992 BaP assessment to  $BW^{3/4}$  in the present assessment should be discussed in the assessment. A comparison of the results of using the two different scaling factors can be easily accomplished by demonstrating how the scaling change impacts the estimate in the 1992 BaP assessment.